

Beyond Fibroids: Association of Hypothyroidism and Thyroid Nodules with Uterine Leiomyoma

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ABSTRACT

Background: Uterine leiomyoma is a common benign gynaecological tumour, and thyroid abnormalities may coexist with leiomyoma, although the association remains uncertain. This study compared hypothyroidism and thyroid nodules in women with leiomyoma and age-frequency-matched controls and examined their relationship with leiomyoma burden.

Methods: This hospital-based case-control study with prospective recruitment was conducted at Santiniketan Medical College and Hospital, West Bengal, from January 2024 to December 2025. One hundred women aged 25–55 years were enrolled, including 50 women with ultrasonographically confirmed leiomyoma and 50 controls without leiomyoma. Participants underwent clinical assessment, pelvic and thyroid ultrasonography, and serum Thyroid-stimulating hormone (TSH) estimation. Associations were assessed using chi-square/Fisher's exact tests and univariate logistic regression; $p < 0.05$ was considered significant.

Results: Hypothyroidism was more prevalent in cases than controls (34% vs. 10%; OR=4.64, 95% CI: 1.55–13.84; $p=0.006$). Thyroid nodules were also more common in cases (32% vs. 12%; OR=3.45, 95% CI: 1.22–9.76; $p=0.020$). Within the leiomyoma group, hypothyroidism was associated with multiple rather than single leiomyomas (46.4% vs. 18.2%; $p=0.021$) and increased with leiomyoma size (16.7%, 25%, and 55.6% for <3 , 3–5, and >5 cm, respectively; $p=0.034$). Thyroid nodule number and size were not significantly associated with leiomyoma characteristics.

Conclusion: Women with uterine leiomyoma had higher prevalences of hypothyroidism and thyroid nodules than controls. Hypothyroidism was also associated with greater leiomyoma number and size. These findings indicate an association but do not establish causality; larger prospective studies with multivariable adjustment are needed.

Key-words: Uterine leiomyoma; Hypothyroidism; Thyroid nodules; Thyroid-stimulating hormone (TSH)

INTRODUCTION

Uterine leiomyomas, commonly referred to as fibroids, are the most frequently encountered benign tumours of the female reproductive system and affect a substantial proportion of women during their reproductive years. Epidemiological studies estimate that up to 70–80% of

women develop fibroids by the age of 50 years. Although many lesions remain clinically silent, symptomatic leiomyomas may result in heavy menstrual bleeding, pelvic pain or pressure, reproductive dysfunction, and adverse pregnancy outcomes. The aetiology of uterine leiomyomas is complex and involves the interaction of genetic susceptibility, endocrine influences, and environmental factors that collectively contribute to tumour initiation and growth ^[1].

Histologically, uterine leiomyomas arise from monoclonal proliferation of smooth muscle cells within the myometrium and are characterized by excessive accumulation of extracellular matrix together with

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varying amounts of fibrous connective tissue. Their development has been associated with multiple risk factors, including Black ethnicity, early menarche, elevated body mass index, and prolonged exposure to ovarian steroid hormones. Leiomyoma tissue expresses higher concentrations of oestrogen and progesterone receptors than adjacent normal myometrium, indicating enhanced hormonal responsiveness. Consequently, oestrogen and progesterone play central roles in regulating the growth, maintenance, and biological behaviour of these tumours ^[1].

Thyroid nodules are common, with a reported prevalence of almost 25% in the general population, although prevalence varies with age, sex, and other risk factors ^[2]. Most thyroid nodules are benign, but appropriate evaluation remains essential because a minority may harbour malignant disease. Their development is multifactorial and is associated with demographic, environmental, and other clinical factors ^[2].

Interest in the relationship between uterine leiomyomas and thyroid disorders has increased over recent decades. An early investigation published in 1989 demonstrated that women undergoing hysterectomy for uterine fibroids exhibited abnormal responses to thyrotropin-releasing hormone (TRH) stimulation testing more frequently than control subjects. The same study also reported a higher prevalence of thyroid autoantibodies, including antithyroglobulin and antiperoxidase antibodies, suggesting a possible association between uterine leiomyomas and thyroid autoimmunity ^[3]. Subsequent studies have further described increased frequencies of thyroid malignancy ^[4], thyroid nodules ^[5,6], and clinically diagnosed hypothyroidism ^[7] among women with uterine leiomyomas, although the consistency of these findings has varied across different study populations.

Thyroid abnormalities, particularly thyroid enlargement and nodular disease, have increasingly been reported in women with uterine leiomyomas (UL) ^[8,9]. Disturbances in thyroid function, including subclinical hormonal alterations, may adversely affect the hypothalamic–pituitary–ovarian axis, ovarian steroidogenesis, ovulation, and endometrial receptivity. These endocrine changes have been implicated in menstrual irregularities, impaired fertility, and other reproductive disorders,

suggesting that thyroid dysfunction may influence several aspects of female reproductive health ^[10,11].

Among the available laboratory investigations, measurement of serum TSH remains the preferred initial test for assessing thyroid function because alterations in TSH generally occur earlier than changes in circulating triiodothyronine (T3) and thyroxine (T4) concentrations. In addition, TSH demonstrates relatively low biological variability and serves as a reliable indicator of thyroid status in routine clinical practice ^[12]. Experimental and clinical studies have also shown that oestrogen can modulate thyroid physiology by influencing thyroid cell activity and TSH regulation, providing a biologically plausible mechanism or the coexistence of thyroid disorders and oestrogen-dependent gynaecological diseases ^[13,14].

Despite these observations, thyroid dysfunction frequently remains underrecognized in women presenting with gynaecological complaints because many symptoms are nonspecific and may overlap with manifestations of reproductive disorders. Consequently, thyroid function testing is not performed universally, and subtle abnormalities may remain undetected. Furthermore, the available evidence regarding the relationship between serum TSH levels and uterine leiomyoma is limited and has yielded inconsistent findings, making it difficult to establish definitive conclusions regarding their clinical association.

Clarifying the relationship between uterine leiomyoma and thyroid abnormalities may have important clinical implications. Identification of coexisting thyroid dysfunction could facilitate comprehensive patient evaluation, improve individualized management strategies, and potentially contribute to better reproductive and gynaecological outcomes. Therefore, the present study was undertaken to compare thyroid function, as assessed by serum TSH levels, and the prevalence of thyroid nodules in women with ultrasonographically confirmed uterine leiomyoma and age-frequency-matched women without leiomyoma. The study also aimed to examine whether thyroid abnormalities are associated with the number and size of uterine leiomyomas, thereby providing additional evidence regarding the possible endocrine relationship between these conditions.

MATERIALS AND METHODS

Study Design and Setting- This hospital-based case-control study with prospective recruitment was conducted jointly by the Department of Obstetrics and Gynaecology and the Department of Otorhinolaryngology at Santiniketan Medical College and Hospital, Bolpur, West Bengal, India, over a two-year period from January 2024 to December 2025.

Study Population- The study included women attending the Department of Obstetrics and Gynaecology during the study period. Participants were classified into two groups according to the presence or absence of ultrasonographically confirmed uterine leiomyoma:

- **Cases:** Women with ultrasonographically confirmed uterine leiomyoma.
- **Controls:** Age-frequency-matched women without evidence of uterine leiomyoma on pelvic ultrasonography who attended the department for benign gynaecological conditions or routine gynaecological evaluation.

A total of 100 participants were enrolled, comprising 50 cases and 50 controls. Eligible participants were recruited consecutively after screening according to the predefined inclusion and exclusion criteria and after obtaining written informed consent.

Inclusion Criteria

Cases

1. Women aged 25–55 years.
2. Ultrasonographically confirmed uterine leiomyoma.
3. Presence of one or more menstrual symptoms, including heavy menstrual bleeding, dysmenorrhea, irregular menstrual cycles, or abdominopelvic pain.
4. Provision of written informed consent.

Controls

1. Women aged 25–55 years.
2. No evidence of uterine leiomyoma on pelvic ultrasonography.
3. Attendance for benign gynaecological conditions or routine gynaecological evaluation.
4. Frequency-matched to the case group by age category.
5. Provision of written informed consent.

Exclusion Criteria

The following participants were excluded from both groups:

1. Pregnant women.
2. History of hysterectomy or myomectomy.
3. Previous thyroid surgery.
4. Known thyroid malignancy.
5. Current treatment with thyroid hormone replacement or antithyroid medications.
6. Chronic systemic diseases known to affect thyroid function.
7. Use of medications known to interfere with thyroid function tests.
8. Pelvic malignancy.
9. Refusal to participate.

Data Collection- Eligible participants underwent evaluation using a predesigned and structured case record form (CRF). Demographic characteristics, clinical findings, laboratory investigations, and imaging results were recorded.

Demographic information- A comprehensive clinical evaluation was performed, including detailed history taking, general physical examination, systemic examination, thyroid examination, abdominal examination, and gynaecological examination.

Pelvic ultrasonography was performed in all participants. In the case group, the number of uterine leiomyomas and the maximum diameter of the largest leiomyoma (cm) were recorded. In the control group, pelvic ultrasonography confirmed the absence of uterine leiomyoma.

For the purposes of this study, hypothyroidism was defined as a serum TSH concentration above the laboratory reference range (>4 mIU/L). Participants with serum TSH within the reference range (0.4 – 4 mIU/L) were considered euthyroid. No participant had a serum TSH value consistent with hyperthyroidism. High-resolution thyroid ultrasonography was performed by the Department of Otorhinolaryngology. The presence or absence of thyroid nodules was documented. In participants with thyroid nodules, the size of the largest nodule was categorized as <1 cm or ≥ 1 cm, and the number of nodules was recorded as single or multiple.

Statistical Analysis- Data were analysed using IBM SPSS Statistics for Windows, Version 26. Continuous variables were summarized as mean $\pm$ SD or median (IQR), as appropriate, and categorical variables as frequencies and percentages. Between-group comparisons used the independent-samples t-test or Mann–Whitney U test for continuous variables and the chi-square or Fisher’s exact test for categorical variables. Univariate binary logistic regression was used to estimate odds ratios (ORs) with 95% confidence intervals (CIs) for the associations of hypothyroidism and thyroid nodules with uterine leiomyoma. Associations between thyroid abnormalities and leiomyoma characteristics were assessed using chi-square or Fisher’s exact tests. All tests were two-tailed, and $p < 0.05$ was considered statistically significant.

Ethical Considerations- The study protocol was approved by the Institutional Ethics Committee of Santiniketan

Medical College and Hospital before commencement of the study. Written informed consent was obtained from all participants prior to enrolment. Participant confidentiality and data privacy were maintained throughout the study in accordance with institutional ethical guidelines.

RESULTS

A total of 100 women were included in the study, comprising 50 cases (women with ultrasonographically confirmed uterine leiomyoma) and 50 age-frequency-matched controls (women without uterine leiomyoma). The two groups were comparable in age distribution and place of residence. Nineteen participants (38.0%) in each group were aged 25–40 years, while 31 (62%) in each group were aged 41–55 years ($p=1$). Rural residence was reported in 31 (62%) cases and 29 (58%) controls, while urban residence was reported in 19 (38%) and 21 (42%), respectively ($p=0.688$) (Table 1).

Table 1: Participant Demographics

Participant characteristics	Cases (n=50)	Controls (n=50)	Total (n=100)	p-value
Age 25–40 years, n (%)	19 (38)	19 (38)	38 (38)	1.000
Age 41–55 years, n (%)	31 (62)	31 (62)	62 (62)	
Rural residence, n (%)	31 (62)	29 (58)	60 (60)	0.688
Urban residence, n (%)	19 (38)	21 (42)	40 (40)	
Total, n	50	50	100	

Thyroid function differed between the groups. Among cases, 33 (66%) were euthyroid and 17 (34%) were hypothyroid, compared with 45 (90%) and 5 (10%), respectively, among controls. No participant was hyperthyroid. Hypothyroidism was significantly more prevalent among cases (34% vs. 10%; $\chi^2=8.52$, $p=0.004$). In univariate logistic regression, hypothyroidism was

associated with higher odds of uterine leiomyoma (OR=4.64, 95% CI: 1.55–13.84; $p=0.006$). Thyroid nodules were detected in 16 (32%) cases and 6 (12%) controls ($\chi^2=5.40$, $p=0.020$). Univariate logistic regression showed higher odds of leiomyoma among participants with thyroid nodules (OR=3.45, 95% CI: 1.22–9.76; $p=0.020$) (Table 2).

Table 2: Thyroid abnormalities and association with uterine leiomyoma

Thyroid Conditions	Cases (n=50)	Controls (n=50)	OR (95% CI)	p-value
Euthyroid, n (%)	33 (66)	45 (90)	-	0.006
Hypothyroid, n (%)	17 (34)	5 (10)	4.64 (1.55–13.84)	
Thyroid nodule present, n (%)	16 (32)	6 (12)	3.45 (1.22–9.76)	0.020
Thyroid nodule absent, n (%)	34 (68)	44 (88)	-	



Among participants with thyroid nodules, 11 (68.8%) cases and 5 (83.3%) controls had nodules <1 cm, whereas 5 (31.2%) cases and 1 (16.7%) control had nodules ≥1 cm; the difference was not significant

($p=0.481$). Solitary nodules were present in 11 (68.8%) cases and 5 (83.3%) controls, while multiple nodules were present in 5 (31.2%) and 1 (16.7%), respectively ($p=0.640$) (Table 3).

Table 3: Comparison of thyroid nodule size and number among participants with nodules

Thyroid nodule size and number among participants with nodules	Cases (n=16)	Controls (n=6)	Total (n=22)	p-value
Nodule <1 cm, n (%)	11 (68.8)	5 (83.3)	16 (72.7)	0.481
Nodule ≥1 cm, n (%)	5 (31.2)	1 (16.7)	6 (27.3)	
Single nodule, n (%)	11 (68.8)	5 (83.3)	16 (72.7)	0.640
Multiple nodules, n (%)	5 (31.2)	1 (16.7)	6 (27.3)	
Total with nodules, n	16	6	22	-

Among the 50 women with leiomyoma, 22 (44.0%) had a single leiomyoma and 28 (56%) had multiple leiomyomas. Based on maximum diameter, 12 (24%) had

lesions <3 cm, 20 (40%) had lesions measuring 3–5 cm, and 18 (36%) had lesions >5 cm (Table 4).

Table 4: Leiomyoma characteristics (number and size)

Leiomyoma Characteristics	Number of women	Percentage (%)
Single leiomyoma	22	44.0
Multiple leiomyomas	28	56.0
Maximum size <3 cm	12	24.0
Maximum size 3–5 cm	20	40.0
Maximum size >5 cm	18	36.0
Total	50	100.0

Within the leiomyoma group, hypothyroidism was significantly associated with leiomyoma number and size. Four of 22 (18.2%) women with a single leiomyoma were hypothyroid compared with 13 of 28 (46.4%) women with multiple leiomyomas ($\chi^2=5.32$, $p=0.021$).

The proportion of hypothyroidism increased from 16.7% in women with lesions <3 cm to 25% in those with lesions measuring 3–5 cm and 55.6% in those with lesions >5 cm ($\chi^2=6.79$, $p=0.034$) (Table 5).

Table 5: Comparison of leiomyoma burden and thyroid function

Leiomyoma burden according to thyroid function	Euthyroid, n	Hypothyroid, n	Total, n	p-value
Single leiomyoma	18	4	22	0.021
Multiple leiomyomas	15	13	28	
Maximum size <3 cm	10	2	12	0.034
Maximum size 3–5 cm	15	5	20	
Maximum size >5 cm	8	10	18	
Total	33	17	50	

Thyroid nodule prevalence did not differ significantly according to leiomyoma number or size. Nodules were present in 5 (22.7%) women with a single leiomyoma and 11 (39.3%) women with multiple leiomyomas ($\chi^2=1.62$, $p=0.203$). According to maximum leiomyoma size, nodules were present in 2 (16.7%), 6 (30%), and 8

(44.4%) women with lesions <3 cm, 3–5 cm, and >5 cm, respectively ($\chi^2=2.58$, $p=0.275$). Among women with thyroid nodules, thyroid nodule size was not significantly associated with leiomyoma size ($\chi^2=2.31$, $p=0.31$) (Table 6).

Table 6: Comparison of leiomyoma burden and thyroid nodule

Leiomyoma burden and thyroid nodule characteristics	Nodule present	Nodule absent	Total	p-value
Single leiomyoma	5	17	22	0.203
Multiple leiomyomas	11	17	28	
Leiomyoma <3 cm	2	10	12	0.275
Leiomyoma 3–5 cm	6	14	20	
Leiomyoma >5 cm	8	10	18	
Among nodules: leiomyoma <3 cm: nodule <1 cm / ≥ 1 cm	2 / 0		2	0.315
Among nodules: leiomyoma 3–5 cm: nodule <1 cm / ≥ 1 cm	5 / 1		6	
Among nodules: leiomyoma >5 cm: nodule <1 cm / ≥ 1 cm	4 / 4		8	
Total with nodules	16	34	50	

DISCUSSION

The present case-control study evaluated the association between uterine leiomyoma and thyroid abnormalities, specifically hypothyroidism and thyroid nodules, in 100 women. The principal findings were that hypothyroidism and thyroid nodules were more prevalent among women with leiomyoma than among age-frequency-matched controls. In univariate logistic regression, leiomyoma status was associated with higher odds of hypothyroidism (OR=4.64; 95% CI: 1.55–13.84) and thyroid nodules (OR=3.45; 95% CI: 1.22–9.76). Within the leiomyoma group, hypothyroidism was also significantly associated with multiple leiomyomas and with increasing maximum leiomyoma size, whereas thyroid nodule number and size were not significantly associated with leiomyoma characteristics.

The higher prevalence of hypothyroidism among women with uterine leiomyoma is consistent with the possibility of an endocrine relationship between the two conditions. In the present study, hypothyroidism was observed in 34% of women with leiomyoma compared with 10% of controls. The corresponding univariate odds ratio indicates a substantial association; however, the confidence interval is relatively wide, reflecting the small sample size.

These findings are broadly consistent with the study by Ott *et al.*, who reported an association between overt hypothyroidism and uterine leiomyoma, including larger leiomyoma size among affected women [7].

Several biological mechanisms could plausibly link thyroid dysfunction with leiomyoma biology. Thyroid hormones participate in cellular proliferation, differentiation and extracellular-matrix metabolism, while thyroid dysfunction can alter ovarian steroid metabolism, sex hormone-binding globulin and peripheral oestrogen activity [16,17]. Hypothyroidism may also influence thyrotropin-releasing hormone and prolactin pathways, which have been proposed as potential contributors to leiomyoma growth [18]. Because leiomyomas are responsive to oestrogen and progesterone, alterations in endocrine homeostasis could potentially affect tumour growth. These mechanisms, however, remain biologically plausible explanations rather than conclusions established by the present observational study.

The observed association should be interpreted in the context of conflicting evidence. Jung *et al.* reported that uterine fibroids were associated with benign thyroid disorders such as thyroid nodules and goitre, while the association with hypothyroidism was not significant after



adjustment for potential confounders ^[20]. Differences in study design, diagnostic definitions, population characteristics and adjustment for metabolic factors may contribute to the variation between studies.

An additional finding was the association between hypothyroidism and leiomyoma burden. Among women with a single leiomyoma, 18.2% were hypothyroid compared with 46.4% of women with multiple leiomyomas ($p=0.021$). Similarly, the proportion of hypothyroid women increased from 16.7% in the <3 cm group to 55.6% in the >5 cm group ($p=0.034$). These findings suggest an association between hypothyroidism and greater leiomyoma burden. Nevertheless, because these analyses are cross-sectional within the case group, they cannot establish that hypothyroidism causes leiomyoma growth or multiplicity.

Thyroid nodules were also significantly more common in women with leiomyoma than in controls (32% vs. 12%). The univariate logistic regression estimate showed approximately 3.45-fold higher odds of thyroid nodules among women with leiomyoma. This finding is consistent with previous reports describing an association between uterine fibroids and thyroid nodules ^[5,20]. A shared endocrine or molecular environment, including effects related to oestrogen signalling and other growth-regulatory pathways, may provide a possible explanation ^[6,17,21].

In contrast, the present study did not demonstrate significant associations between thyroid nodule characteristics and leiomyoma characteristics. Nodule size and number were not significantly related to the number or size of leiomyomas. Although the prevalence of thyroid nodules appeared to increase from 16.7% in women with leiomyomas <3 cm to 44.4% in those with leiomyomas >5 cm, the association was not statistically significant ($p=0.275$). The relatively small number of participants with thyroid nodules limits the statistical power of these subgroup analyses.

The logistic regression findings quantify the magnitude of the associations observed between uterine leiomyoma and the two thyroid abnormalities. The reported ORs represent univariate associations and should be interpreted as measures of association rather than causal effects.

Clinically, the findings suggest that thyroid abnormalities may be relevant when evaluating women with uterine leiomyoma, particularly those with multiple or larger

lesions. However, the present results are insufficient to recommend universal thyroid screening solely on the basis of leiomyoma. Any clinical screening recommendation should be evaluated in larger, adequately powered prospective studies using clearly defined thyroid diagnostic criteria and appropriate adjustment for confounding factors.

The study has several strengths, including an age-frequency-matched control group and standardized assessment of both uterine leiomyomas and thyroid nodules. Its limitations include the relatively small sample size, hospital-based recruitment, case-control design, and the absence of potentially important variables such as body mass index, parity, family history, iodine intake, thyroid antibody status and reproductive hormone concentrations. These limitations may have introduced residual confounding and limit generalizability. The study therefore demonstrates association rather than causation.

CONCLUSIONS

Women with uterine leiomyoma in this study had higher prevalence of hypothyroidism and thyroid nodules than age-frequency-matched controls. Univariate logistic regression demonstrated higher odds of hypothyroidism and thyroid nodules among women with leiomyoma. Hypothyroidism was additionally associated with greater leiomyoma number and size within the case group. These findings support a possible relationship between thyroid abnormalities and uterine leiomyoma but do not establish causality. Larger prospective studies with individual-level data and multivariable adjustment are required to determine whether these associations persist after accounting for relevant clinical and metabolic confounders. Future research should further evaluate the temporal and biological relationship between thyroid dysfunction and leiomyoma development and progression using larger, multicentre cohorts with standardized assessment of thyroid function, thyroid nodules, and leiomyoma burden. Such studies may help clarify whether thyroid abnormalities have implications for risk stratification or individualized evaluation of women with uterine leiomyoma.

CONTRIBUTION OF AUTHORS

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